IN THE CLAIMS

The following claims with parenthetical status notations have been presented previously. An instruction line precedes each claim that is amended by the instant paper.

1. [PREVIOUSLY CANCELLED]

2. [PREVIOUSLY CANCELLED]

3. [PREVIOUSLY CANCELLED]

4. [PREVIOUSLY CANCELLED]

5. [PREVIOUSLY CANCELLED]

6. [PREVIOUSLY CANCELLED]

7. [PREVIOUSLY CANCELLED]

8. [PREVIOUSLY CANCELLED]

9. [PREVIOUSLY CANCELLED]

10. [PREVIOUSLY CANCELLED]

11. [PREVIOUSLY CANCELLED]

12. [PREVIOUSLY CANCELLED]

13. [PREVIOUSLY CANCELLED]

Please **amend** claim 14 as follows:

14. [CURRENTLY AMENDED] An *in vitro* method for producing ~~dendritic~~ Langerhans -type dendritic cells, said method comprising:

a. culturing cells selected from the group consisting of peripheral blood monocytes and bone marrow cells in a medium containing platelets ~~obtained from the same species or phylogenetically close species~~; and

b. incubating the culture at about ~~30~~30°C to about 40°C for a period sufficient to enable formation of mature ~~dendritic~~ Langerhans -type dendritic cells,

wherein the medium omits an exogenous cytokine.

15. [PREVIOUSLY ADDED] The method as claimed in claim **14**, wherein the exogenous cytokine is granulocyte macrophage colony stimulating factor or interleukin-4.

16. [PREVIOUSLY ADDED] The method as claimed in claim **14** wherein the medium comprises RPMI-1640.

17. [PREVIOUSLY ADDED] The method as claimed in claim **14** wherein the cells are cultured for a period of about 2 to about 8 days.

18. [PREVIOUSLY ADDED] The method as claimed in claim **14** wherein the medium further comprises fetal calf serum.

19. [PREVIOUSLY ADDED] The method as claimed in claim **18**, wherein the medium contains at least about 2% fetal calf serum.

20. [PREVIOUSLY ADDED] The method as claimed in claim **19**, wherein the fetal calf serum is about 10%.

Please **amend** claim 21 as follows:

21. [CURRENTLY AMENDED] The method as claimed in claim **14** wherein human platelets are added to the medium to develop ~~dendritic~~ Langerhans -type dendritic cells.

Please **amend** claim 22 as follows:

22. [CURRENTLY AMENDED] The method as claimed in claim **14** wherein rat platelets are added to the medium

containing mice blood cells to develop ~~dendritic~~ Langerhans -type dendritic cells.

Please **amend** claim 23 as follows:

23. [CURRENTLY AMENDED] A method for producing ~~dendritic~~ Langerhans -type dendritic cells *in vitro* comprising:

a. preparing peripheral blood monocytes and/or bone marrow cells; and

b. culturing the peripheral blood monocytes or the bone marrow cells with platelets of the same species ~~or phylogenetically close species~~ in a culture medium lacking an exogenous cytokine such that ~~dendritic~~ Langerhans -type dendritic cells are produced.

Please **amend** claim 24 as follows:

24. [CURRENTLY AMENDED] The method of claim **23** further comprising analyzing the morphology of human ~~dendritic~~ Langerhans -type dendritic cells produced.

Please **amend** claim 25 as follows:

25. [CURRENTLY AMENDED] The method of claim **23** further comprising analyzing the ~~dendritic~~ Langerhans -type dendritic cells produced by flow cytometry.

Please **amend** claim 26 as follows:

26. [CURRENTLY AMENDED] The method of claim **23** wherein the peripheral blood monocytes, the platelets, and the ~~dendritic~~ Langerhans -type dendritic cells produced are human.

Please **amend** claim 27 as follows:

27. [CURRENTLY AMENDED] The method of claim **23** wherein the bone marrow cells are mouse bone marrow cells, the platelets are rat platelets, and the ~~dendritic~~ Langerhans -type dendritic cells produced are mouse ~~dendritic~~ Langerhans -type dendritic cells.

Please **add** new claims 28-33 as follows:

28. [NEW] An *in vitro* method for producing Langerhans-type dendritic cells, said method comprising:

a. culturing cells selected from the group consisting of peripheral blood monocytes and bone marrow cells in a medium containing platelets; and

b. incubating the culture at about 30°C to about 40°C for a period sufficient to enable formation of mature Langerhans-type dendritic cells.

29. [NEW] A method for producing Langerhans-type dendritic cells *in vitro* comprising:

a. preparing peripheral blood monocytes and/or bone marrow cells; and

b. culturing the peripheral blood monocytes or the bone marrow cells with platelets of the same species in a culture medium such that Langerhans-type dendritic cells are produced.

30. [NEW] A method for producing Langerhans-type dendritic cells *in vitro* comprising:

a. preparing peripheral blood monocytes and/or bone marrow cells; and

b. culturing the peripheral blood monocytes or the bone marrow cells with platelets in a culture medium such that Langerhans-type dendritic cells are produced,

wherein the peripheral blood monocytes and/or bone marrow cells and the platelets may be independently selected from the group of rat cells and mouse cells.

31. [NEW] The method of claim 30, wherein the culture medium lacks an exogenous cytokine.

32. [NEW] A method for producing mature dendritic cells *in vitro* comprising:

a. preparing peripheral blood monocytes and/or bone marrow cells; and

b. culturing the peripheral blood monocytes or the bone marrow cells with platelets of the same species in a culture medium such that mature dendritic cells are produced,

wherein more than about 50% of the mature dendritic cells have dendritic processes and display reactivity to anti-HLA-DR, anti-CD40, and anti-CD86 monoclonal antibodies and less than about 20% of the mature

dendritic cells display reactivity to anti-CD1a, anti-CD80, and anti-CD83 monoclonal antibodies.

33. [NEW] The method of claim 32, wherein the culture medium lacks an exogenous cytokine.

## REMARKS

This paper is being filed in response to the Office Action dated April 23, 2003 that was issued in connection with the above-identified patent application. Applicants also enclose herewith a Supplemental Information Disclosure Statement, Form PTO-1449, and copies of 16 documents. Applicants respectfully request reconsideration of the instant application in view of the amendments and remarks presented herein.

Claims 14-33 are pending in the instant application. Claims 14 and 21-27 have been amended. These amendments are fully supported by the specification, *inter alia*, at page 1, line 22 to page 2, line 1 and page 3, lines 2-8 and, therefore, do not constitute new matter. Claims 28-33 have been added. New claims 28-29 are fully supported by the specification, *inter alia*, at page 3, lines 2-8 and claim 1. New claims 30-31 are fully supported by the specification, *inter alia*, at page 4, lines 14-21, Example 4, and page 8, line 23 to page 9, line 15. New claims 32-33 are fully supported by the specification, *inter alia*, at page 8, lines 15-22. Therefore, new claims 28-33 do not constitute new matter.

As a preliminary matter, Applicants thank the Examiner for withdrawing the restriction requirement.

The Examiner has stated that a paper submitted on June 4, 2002 indicates that an Information Disclosure Statement was submitted, but that no Form PTO-1449 or documents were received. Applicants and their Attorneys have checked their records as well as the Patent and Trademark Office Patent Application Information Retrieval system, but have not found any record of a document filed on that date. However, an Information Disclosure Statement was filed on June 1, 2001, a copy of which is enclosed herewith. *See also* PAIR print-out dated June

24, 2003. Applicants also enclose herewith a Supplemental Information Disclosure Statement, Form PTO-1449, and copies of 16 cited documents.

Claims 14-27 have been rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite for reciting the term "dendritic Langerhans type cells." The Examiner has alleged that it is unclear what separates a Langerhans cell from "dendritic Langerhans type cells."

Applicants traverse this rejection and assert that claims 14-27, as amended herein, are clear and definite. One of ordinary skill in the art will readily appreciate that Langerhans cells are one type of immature dendritic cell. Since Applicants are entitled to be their own lexicographer, *see e.g.* MPEP §2173.01, Applicants have coined the term "dendritic Langerhans type cells" to describe and define the cells of the invention. The specification clearly indicates that these cells are mature dendritic cells that are derived from Langerhans cells. *See e.g.* page 1, line 22 to page 2, line 1 and page 3, lines 2-8. Nevertheless, without modifying the scope of the claimed invention, Applicants have substituted the term "Langerhans-type dendritic cell" to improve the clarity of the claims.

Claim 14-27 have also been rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite for reciting the term "phylogenetically close species." The Examiner has acknowledged that the specification discloses that rats and mice are phylogenetically close species, but alleged that it is unclear what other pairs of species would be considered close.

Applicants traverse this rejection and assert that claims 14-27, as amended herein, and claims 28-33 are clear and definite. Claims 14 and 23 have been amended to omit this term. Applicants, therefore, respectfully request withdrawal of this rejection.

Claim 14-27 have also been rejected under 35 U.S.C. § 112, first paragraph as allegedly drawn to subject matter that was not sufficiently described in the specification to

enable one of ordinary skill in the art to make and use the claimed invention. The examiner has alleged that the art recognizes a bright line of demarcation between mature dendritic cells and immature Langerhans cells wherein mature dendritic cells, but not immature Langerhans cells, express high levels of CD80, CD83, CD86, and MHC class II (HLA-DR) and low levels of CD1a. *See* Paper No. 7, Office Action dated April 23, 2003, page 3, lines 15-31 (citing Steinman, *Fundamental Immunology*, Paul, ed. 1999 (hereinafter "Steinman"). The Examiner concluded, therefore, that it is allegedly unclear exactly what type of cell is produced by the methods of the invention such that one of ordinary skill in the art would have to engage in undue experimentation to practice the invention.

Applicants traverse this rejection and assert that the Examiner has failed to satisfy the burden to establish a reasonable basis to question the enablement provided for the claimed invention. *See* MPEP § 2164.04 (citing In re Wright, 999 F.2d 1557, 1562 (Fed. Cir. 1993). Prior to addressing the question of enablement, the claims must be construed. If a claim term is susceptible to more than one meaning, the Examiner is to select the definition to be used in examining the application and "explicitly set forth the meaning of the term ... when writing an Office Action." *See* MPEP § 2164.04, first paragraph. As noted above, Applicants are entitled to be their own lexicographer and have defined the terms "dendritic Langerhans type cells" and "Langerhans-type dendritic cell" to mean cells with the features described, *inter alia*, at page 8, lines 15-22 and figure 2. Having thus construed the claims, the Examiner is obligated to provide a reasonable explanation for why the claimed methods are not adequately enabled by the disclosure. *See* MPEP § 2164.04, second paragraph. In the instant case, the Examiner must provide a reasonable explanation as to why one of ordinary skill in the art would be unable to prepare cells having the described phenotype using the described and claimed methods. Instead

of providing such an explanation, the Examiner has merely alleged that the term "dendritic Langerhans type cells" is susceptible to more than one meaning. However, the ability to attach a label of "mature" or "immature" to the cells produced according to a particular classification scheme does not impair the ability of underlying method to reliably and reproducibly yield the cells with the disclosed expression pattern. Absent such a connection, Applicants respectfully assert that the Examiner has failed to satisfy the burden of showing that one of ordinary skill in the art could not produce cells highly reactive to anti-HLA-DR, anti-CD40, and anti-CD86 while having only weak reactivity to anti-CD1a, anti-CD1b, CD80 and CD83.

Applicants assert that the specification clearly describes methods of preparing cells having the disclosed cytological features including starting materials, culture media composition, and incubation temperature and atmosphere. *See e.g.* Examples 1-6. The descriptions are provided in terms that would allow one of ordinary skill in the art to culture cells accordingly. Therefore, the specification enables one of ordinary skill in the art to practice the claimed methods for producing Langerhans-type dendritic cells.

Applicants further assert that art does not recognize the bright line of demarcation between immature and mature dendritic cells. Dendritic cells possess a heterogeneous haemopoeitic lineage that, together with the culture conditions, influences the morphology and immunological reactivity of the resulting cells. *See e.g.* Schoppet M et al., 2003, *Arch Pathol Lab Med.* **127**:98-101. Applicants respectfully invite the Examiner's attention to Palucka et al. which shows that cell culture conditions may directly influence the expression of CD1a and CD83. *See* Palucka KA et al., 1998, *J. Immunol.* **160**:4587-4595, paragraph bridging pages 4590-4592.

In summary, no reasonable explanation has been provided why the claimed methods cannot be expected to produce cells as described nor does the art recognize a bright line maturity test as alleged. In addition, the specification provides clear direction to one skilled in the art how to prepare Langerhans-type dendritic cells. Therefore, Applicants respectfully request withdrawal of this rejection.

In light of the foregoing amendments and remarks, Applicants believe that the instant application is in condition for allowance. Accordingly, Applicants respectfully solicit prompt favorable action on the instant application.

Applicants enclose herewith the fee required pursuant to 37 C.F.R. §§ 1.16(b) and 1.17(p). Applicants do not believe that any additional fee is required with this submission. Nevertheless, any required fees not enclosed herewith may be charged to Deposit Account No. 02-4377. Two copies of this page are enclosed.

Respectfully submitted,

July 23, 2003

Rochelle K. Seide
PTO Reg. No. 32,300
Attorneys for Applicants

Guy F. Birkenmeier
PTO Reg. No. 52,622
Agent for Applicants

BAKER BOTTS, L.L.P.
30 Rockefeller Plaza
New York, NY 10112
(212) 408-2500

Enclosures